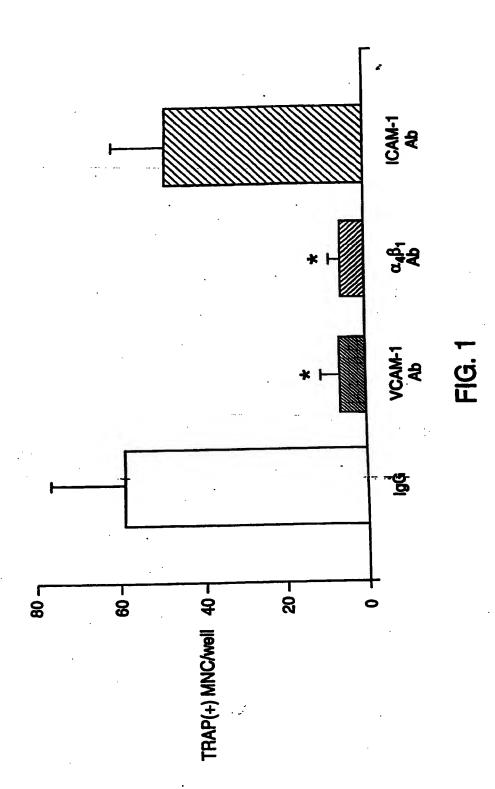
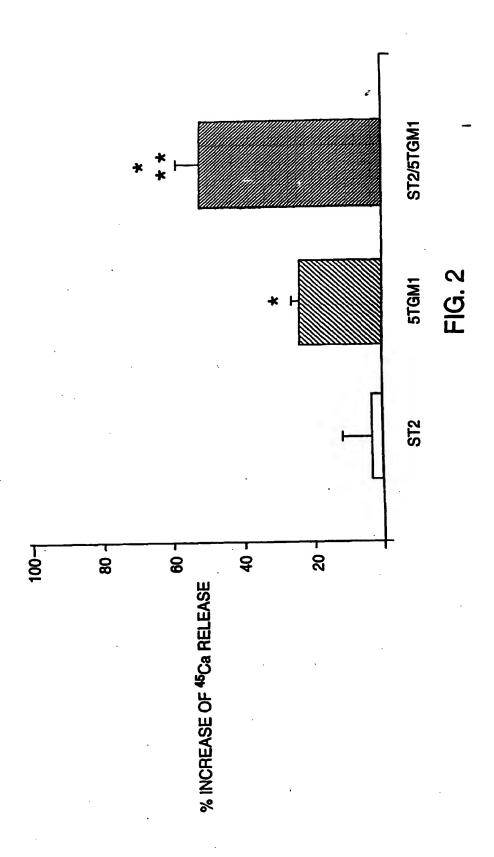
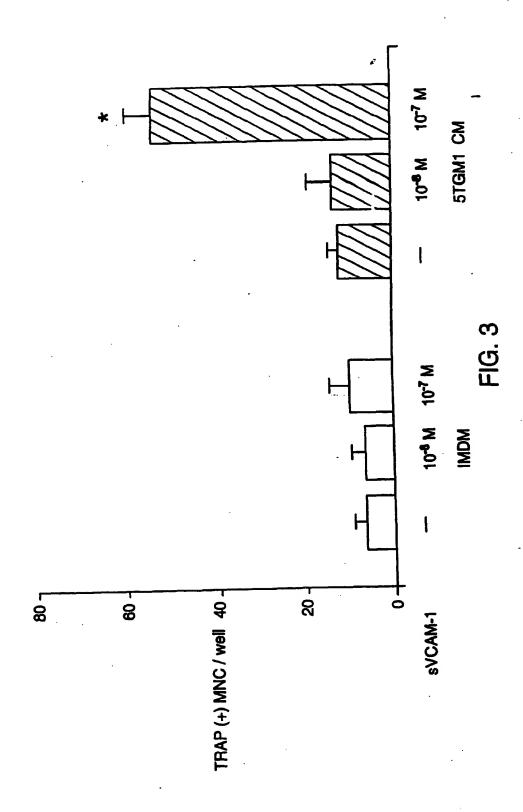
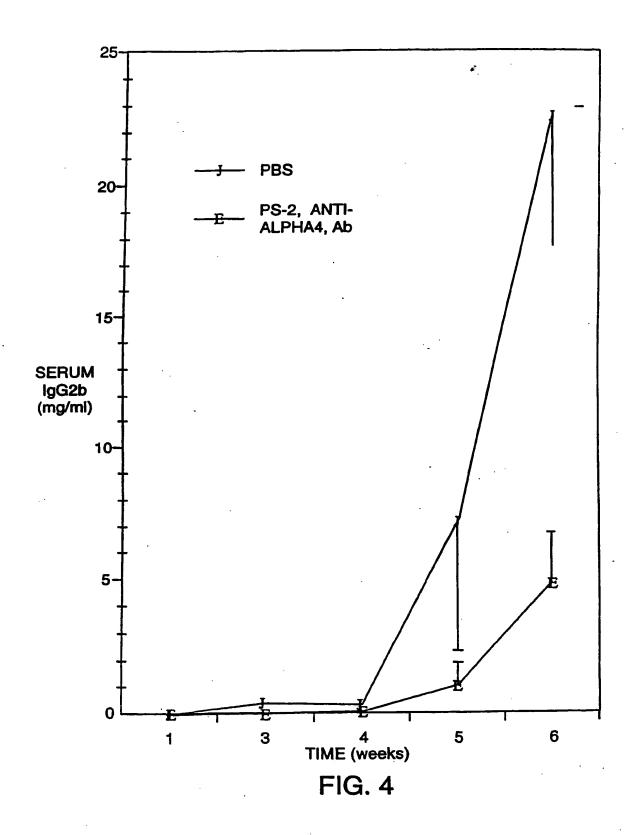
Docket No: A061CIP1
Application No.: 09/943,659 - Confirmation No.: 2421
Inventor: MUNDY et al.
Title: Methods of Treating Multiple Myeloma and
Myeloma-Induced Bone Resorption Using Integrin
Antagonists



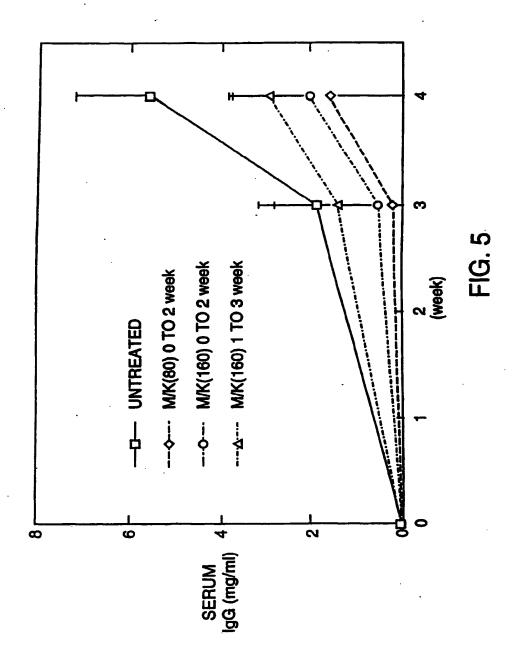
Docket No: A061CIP1
Application No.: 09/943,659 -Confirmation No.: 2421
Inventor: MUNDY et al.
Title: Methods of Treating Multiple Myeloma and
Myeloma-Induced Bone Resorption Using Integrin
Antagonists



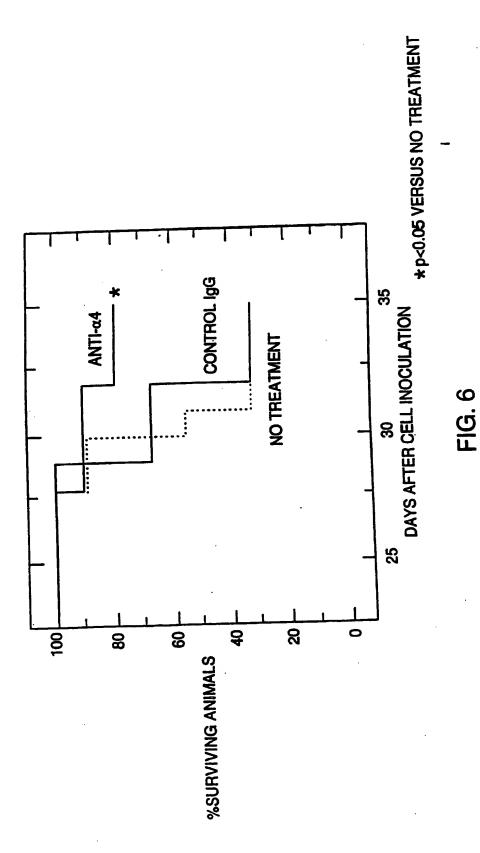




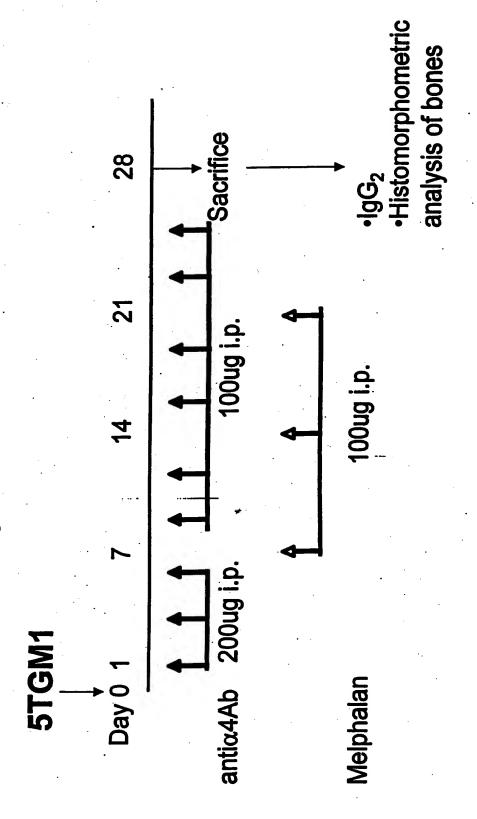
Docket No: A061CIP1
Application No.: 09/943,659 -Confirmation No.: 2421
Inventor: MUNDY et al.
Title: Methods of Treating Multiple Myeloma and
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Antagonists



Docket No: A061CIP1
Application No.: 09/943,659 -Confirmation No.: 2421
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Antagonists

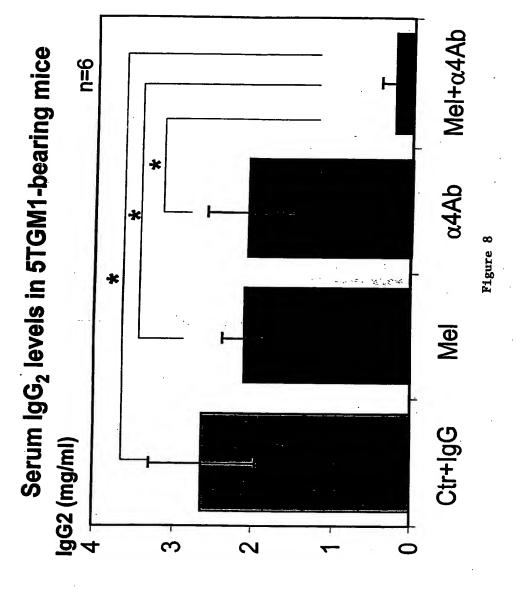


Experimental Protocol

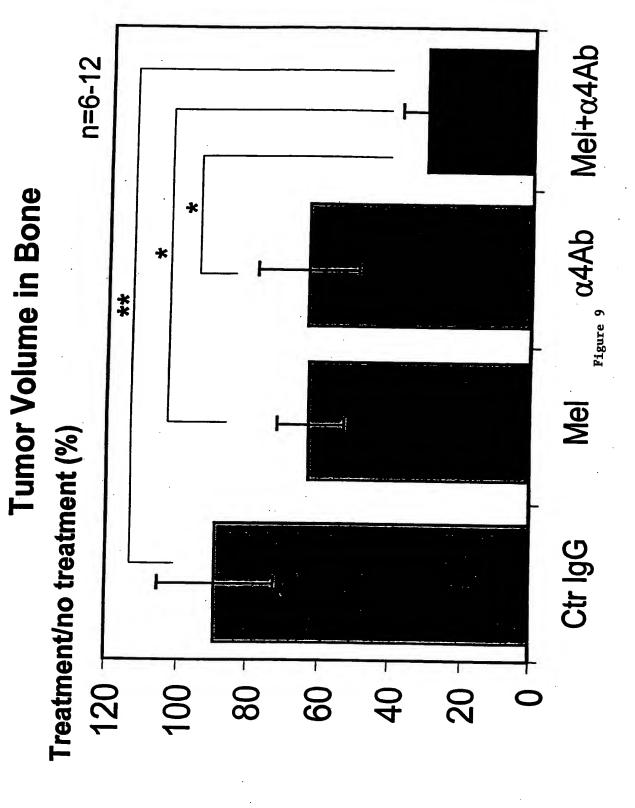


Docket No: A061CIP1
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Title: Methods of Treating Multiple Myeloma and

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Docket No: A061CIP1
Application No.: 09/943,659 -Confirmation No.: 2421
Inventor: MUNDY et al.
Title: Methods of Treating Multiple Myeloma and
Myeloma-Induced Bone Resorption Using Integrin
Antagonists

EFFECT OF PS/2 mAb TREATMENT ON SPLEEN WEIGHT

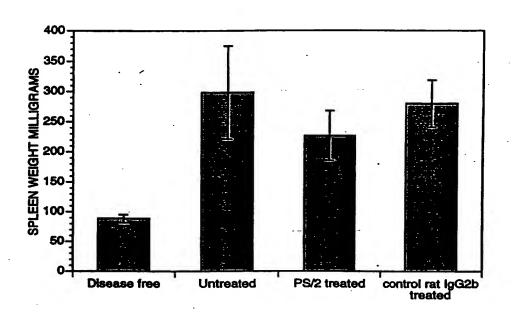
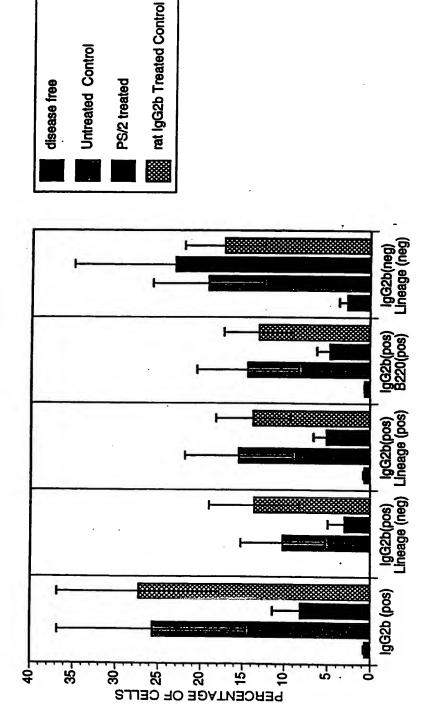


Figure 10

Docket No: A061CIP1
Application No.: 09/943,659 -Confirmation No.: 2421
Inventor: MUNDY et al.
Title: Methods of Treating Multiple Myeloma and
Myeloma-Induced Bone Resorption Using Integrin
Antagonists

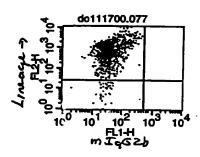
EFFECT OF PS/2 TREATMENT ON SPLENOCYTES IN MICE WITH 5TGM1 MYELOMA



Pigure 11

EFFECT OF PS/2 mAb TREATMENT ON SPLENOCYTE FACS PROFILE

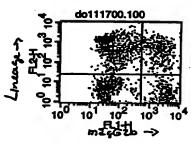
DISEASE FREE



File: do111700.077 Acquisition Date: 17-Nov-00
Gate: G1 Gated Events: 9624
Total Events: 10707 Quad Location: 523, 25

Quad Events % Gated % Total X Mean Y Mean UL 9499 98.70 88.72 37.11 UR 3 0.03 0.03 5084.96 ш 122 1.27 1.14 31.88 LR 0.00 0.00

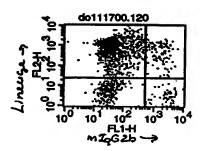
UNTREATED



File: do111700.100 Acquisition Date: 17-Nov-00
Gate: G1 Gated Events: 9526
Total Events: 11100 Quad Location: 523, 25

Quad Events % Gated % Total X Mean Y Mean 4959 UL. 52.06 44.68 84.30 1023.41 UR 1388 14.57 12.50 2377.81 704.20 ш 2163 22.71 19.49 50.53 6.64 1016 10.67 9.15 3619.03

PS/2 TREATED

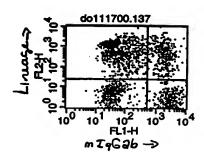


File: do111700.120 Gate: G1 Total Events: 10934

Acquisition Date: 17-Nov-00 Gated Events: 9561 Quad Location: 523, 25

Qu	ad	Events	% Gated	% Total	X Mean	Y Mean
	UL.	7868	82.29	71.96	58.00	1139.33
(JR	310	3.24	2.84	1922.82	897.47
	ш	1171	12.25	10.71	42,10	8.17
1	LR	212	2.22	1.94	3153.17	3.62

rat IgG2b TREATED



File: do111700.137 Gate: G1

Total Events: 10970

1597

LR

7 Acquisition Date: 17-Nov-00
Gated Events: 9595
Ouad Location: 523, 25

14.56 3286,15

2.68

Quad Events % Gated % Total X Mean Y Mean UL 4910 51.17 44.76 84.95 975.19 UR 1384 14.42 12.62 1937.36 694.49 ш 1704 17.76 15.53 48.67 7.00

Figure 12

16.64

EFFECT OF PS/2 mAb TREATMENT ON SPEEN TUMOR BURDEN

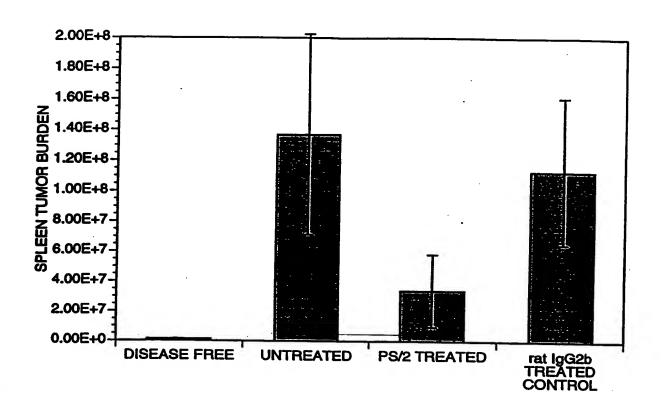


Figure 13

Docket No: A061CIP1
Application No.: 09/943,659 -Confirmation No.: 2421
Inventor: MUNDY et al.
Title: Methods of Treating Multiple Myeloma and
Myeloma-Induced Bone Resorption Using Integrin
Antagonists

rat IgG2b Treated Control Untreated Control PS/2 treated disease free EFFECT OF PS/2 mAB TREATMENT ON BONE MARROW CELLS lgG2b(neg) IN MICE WITH 5TGM1 MYELOMA lgG2b(pos) IgG2b(pos) Lineage (neg) Lineage (pos) lgG2b (pos) 90 **₽** 101 င္ထ 20 PERCENTAGE OF CELLS

Figure 14

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Docket No: A061CIP1
Application No.: 09/943,659 -Confirmation No.: 2421
Inventor: MUNDY et al.
Title: Methods of Treating Multiple Myeloma and
Myeloma-Induced Bone Resorption Using Integrin
Antagonists

EFFECT OF PS/2 TREATMENT ON BONE MARROW TUMOR BURDEN mlgG2b POSITIVE CELLS

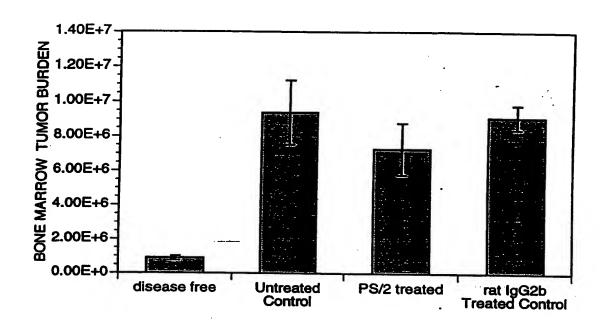


Figure 15

EFFECT OF PS/2 mAb TREATMENT ON 5TGM1 CELLS IN THE BLOOD

14-

12-

Docket No: A061CIP1
Application No.: 09/943,659 -Confirmation No.: 2421
Inventor: MUNDY et al.
Title: Methods of Treating Multiple Myeloma and
Myeloma-Induced Bone Resorption Using Integrin

Antagonists

rat IgG2b Treated Control Untreated Control disease free PS/2 treated

lgG2b(pos) Lineage (pos) IgG2b(pos) Lineage (neg) lgG2b (pos)

PERCENTAGE OF CELLS

2

Figure 16

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The time that the

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Docket No: A061CIP1
Application No.: 09/943,659 -Confirmation No.: 2421
Inventor: MUNDY et al.
Title: Methods of Treating Multiple Myeloma an
Myeloma-Induced Bone Resorption Using Integrin
Antagonists .

EFFECT OF PS/2 TREATMENT ON BLOOD CHEMISTRY

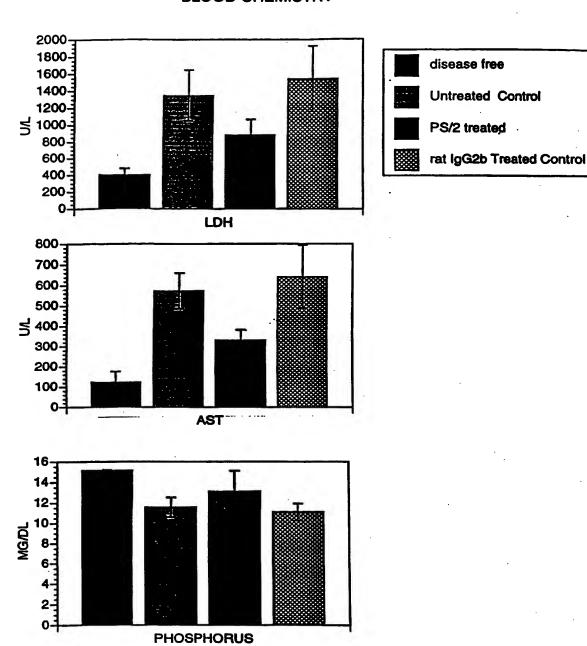
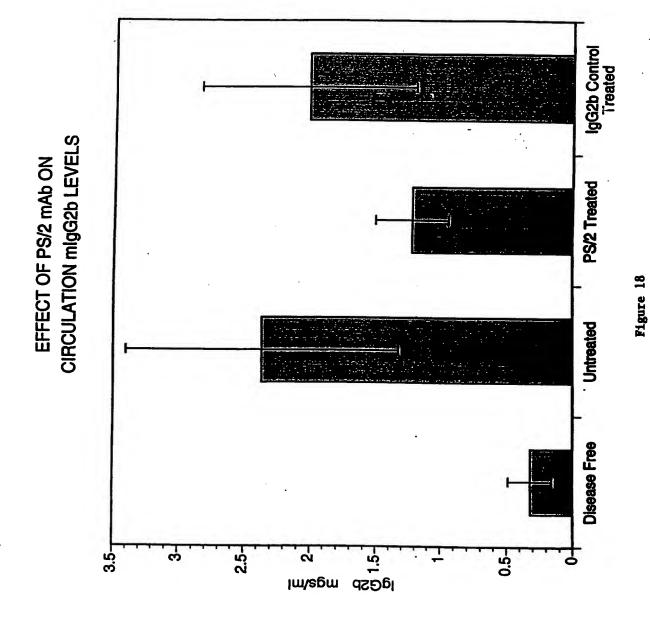


Figure 17



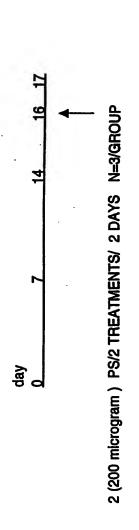
Antagonists

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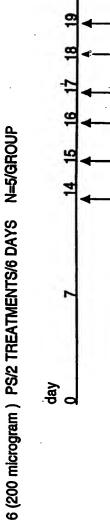
The that the that who

C57/BI KaLwRaj MULTIPLE MYELOMA MODEL ACUTE TREATMENT PROTOCOLS

1 (200 microgram) PS/2 TREATMENT / 1 DAY N=3/GROUP

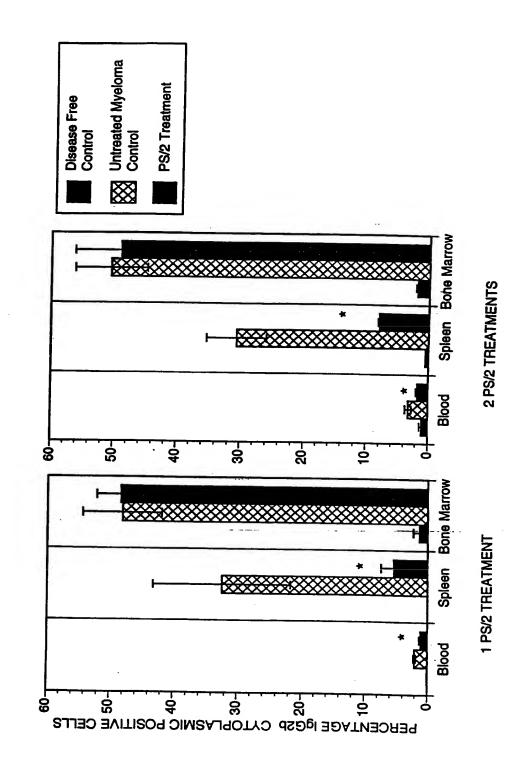






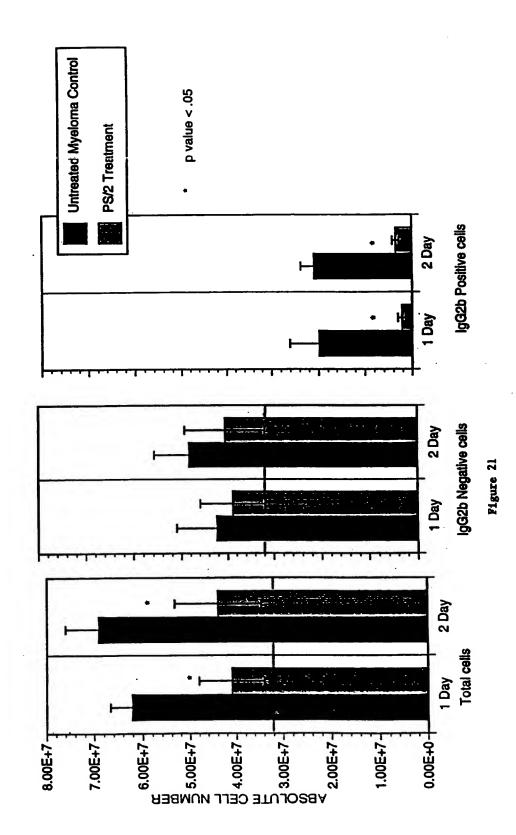
Pigure 19

EFFECT OF PS/2 TREATMENT ON 19G2b POSITIVE CELLS ACUTE TREATMENT MODEL

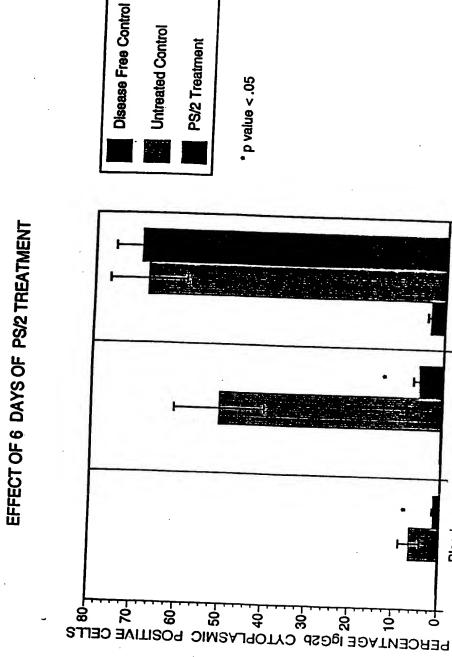


Pigure 20

EFFECT OF ANTI VLA-4 ANTIBODY PS/2 ON TUMOR BURDEN IN SPLEEN



The first from from the Maria Maria

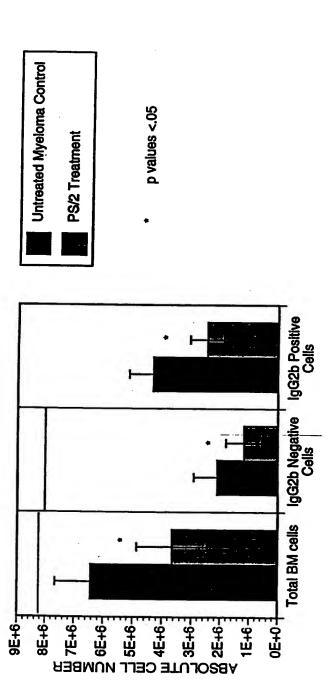


dgure ?

Вопе Маггом

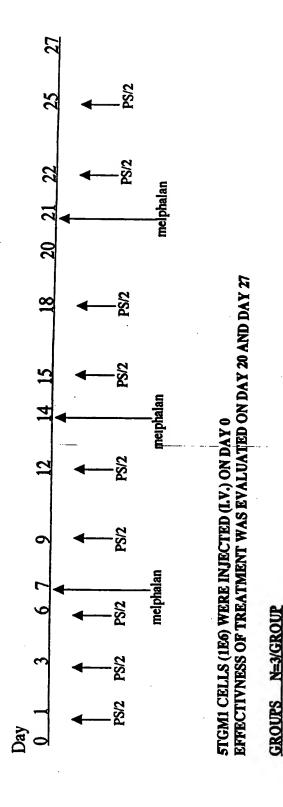
Blood

EFFECT OF 6 DAYS OF PS/2 TREATMENT ON BONE MARROW CELLS



Pigure 2

C57/BIKaLwRaj MODEL OF MULTIPLE MYELOMA COMBINATION TREATMENT WITH PS/2 AND MELPAHLAN



MELPHALAN AND PS/2 MELPAHLAN AND rigG2b ISOTYPE CONTROL

Figure 24

MELPHALAN TREATMENT-100 MICROGRAMS/INJECTION

UNTREATED MYELOMA CONTROL

DISEASE FREE CONTROL

PS/2 TREATMENT --- 100 MICROGRAMS/INJECTION

Docket No: A061CIP1
Application No.: 09/943,659 -Confirmation No.: 2421
Inventor: MUNDY et al.
Title: Methods of Treating Multiple Myeloma and
Myeloma-Induced Bone Resorption Using Integrin
Antagonists

EFFECT OF TREATMENT ON mIgG2b PLASMA LEVELS

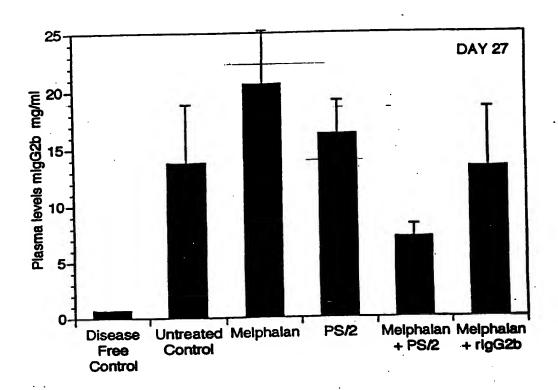


Figure 25

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Docket No: A061CIP1
Application No.: 09/943,659 -Confirmation No.: 2421
Inventor: MUNDY et al.
Title: Methods of Treating Multiple Myeloma and
Myeloma-Induced Bone Resorption Using Integrin
Antagonists

EFFECT OF TREATMENT ON MYELOMA CELLS AT DAY 27

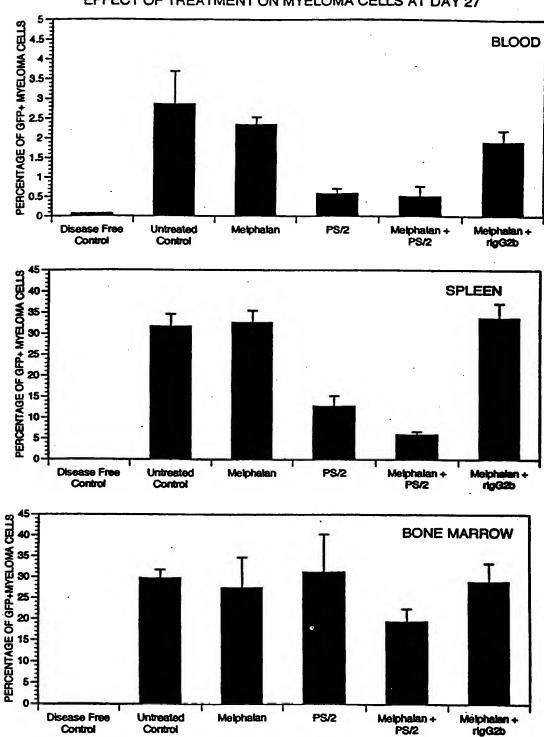
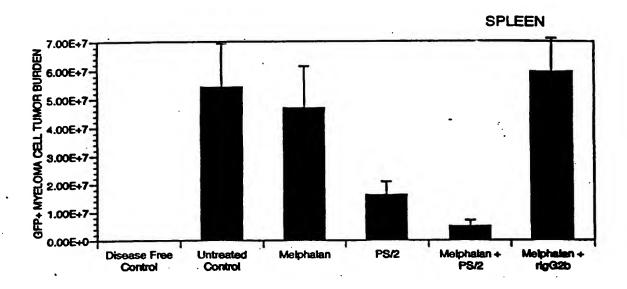


Figure 26

EFFECT OF TREATMENT ON TUMOR BURDEN AT DAY 27



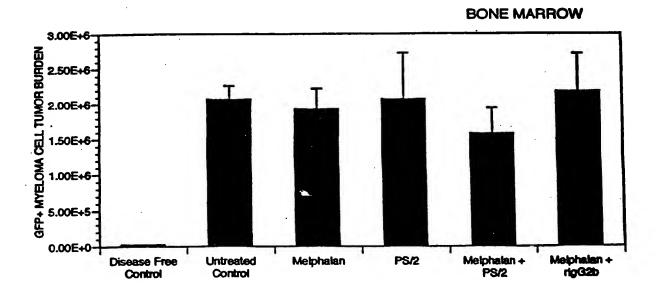


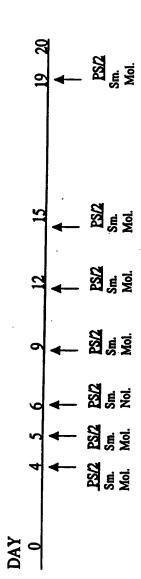
Figure 27

Docket No: A061CIP1 Application No.: 09/943,659 -Confirmation No.: 2421 Inventor: MUNDY et al. Title: Methods of Treating Multiple Myeloma and Myeloma-Induced Bone Resorption Using Integrin Antagonists ...

	Day 20	day 27	
	PS/2 Plasma levels	PS/2 Plasma levels	
8-PS/2	none detected	none detected	
9-PS/2	none detected	none detected	
10-PS/2	none detected	none detected	
11-melphalan+PS/2	none detected	none detected	
12-melphalan+PS/2	3.7 μg/ml	none detected	
13-melphalan+PS/2	none detected	none detected	

III with these thest that with the

C57/BIKaLwRaj MODEL OF MULTIPLE MYELOMA PS/2 AND ANTI VLA4 SMALL MOLECULE LONG TERM TREATMENT



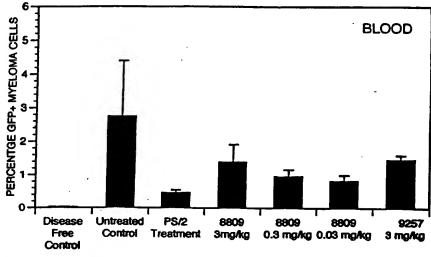
BFFECTIVNESS OF TREATMENT WAS EVALUATED ON DAY 20 STGM1 CELLS (1E6) INJECTED(I.V.) ON DAY 0

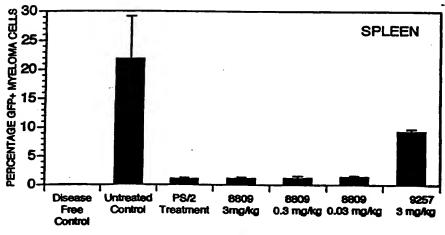
Sm. Mol . 8809--3 mg/kg, 0.3 mg/kg or 0.03 mg/kg Sm. Mol. 9257 CONTROL -- 3 mg/kg UNTREATED MYELOMA CONTROL PS/2 -- 100 micrograms/injection DISEASE FREE CONTROL GROUPS N=2/GROUP

Figure 29

Antagonists

EFFECT OF LONG TERM TREATMENT ON MYELOMA CELLS





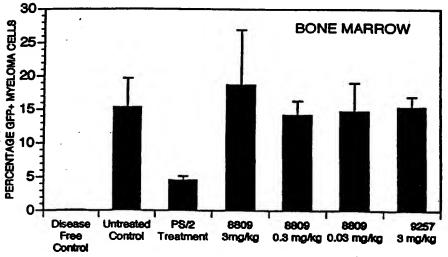


Figure 30

Docket No: A061CIP1
Application No.: 09/943,659 - Confirmation No.: 2421
Inventor: MUNDY et al.
Title: Methods of Treating Multiple Myeloma and
Myeloma-Induced Bone Resorption Using Integrin
Antagonists

EFFECT OF LONG TERM TREATMENT ON TUMOR BURDEN

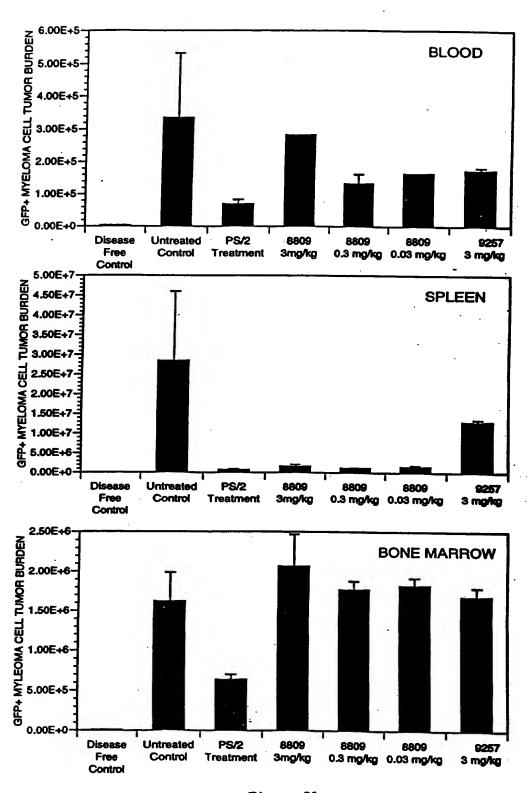


Figure 31

Docket No: A061CIP1
Application No.: 09/943,659 -Confirmation No.: 2421
Inventor: MUNDY et al.
Title: Methods of Treating Multiple Myeloma and
Myeloma-Induced Bone Resorption Using Integrin

C57/BIKaLwRaj MODEL OF MULTIPLE MYELOMA PS/2 AND ANTI VLA4 SMALL MOLECULE ACUTE TREATMENT

PS/2 PS/2 PS/2 Sm. Mol. Sm. Mol. Sm. Mol. PS/2 PS/2

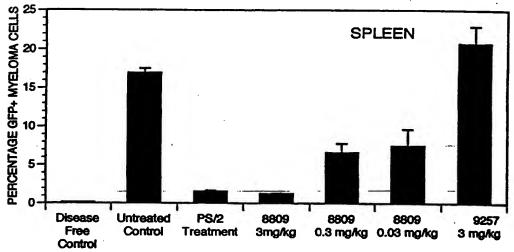
DAY

5TGM1 CELLS (1E6) INJECTED(I.V.) ON DAY 0
PS/2 WAS GIVEN ON DAYS 15,16,17,18,19 AND 20
SMALL MOLECULE WAS GIVEN ON DAYS 15, 16 AND 17
EFFECTIVNESS OF TREATMENT WAS EVALUATED ON DAY 21

GROUPS N=2/GROUP
DISEASE FREE CONTROL
UNTREATED MYELOMA CONTROL
PS/2 --100 micrograms/injection
8809--3 mg/kg, 0.3 mg/kg or 0.03 mg/kg
9257 CONTROL -- 3 mg/kg

Figure 32

EFFECT OF ACUTE TREATMENT ON MYELOMA CELLS PERCENTAGE GFP+ MYELOMA CELLS **BLOOD** 3.5 3 2.5 2 1.5 0.5 0 Disease Untreated **PS/2** 8809 8809 8809 9257 Free Control Treatment 3mg/kg 0.3 mg/kg 0.03 mg/kg 3 mg/kg Control



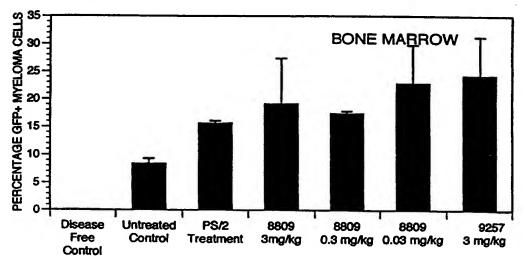
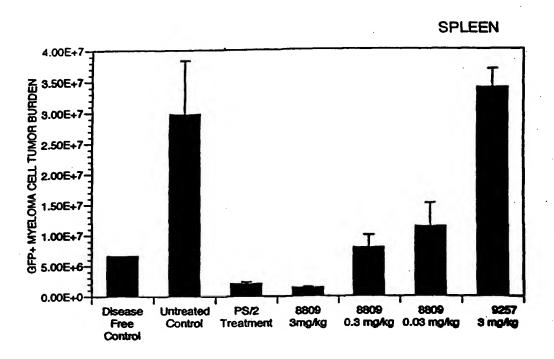


Figure 33

Docket No: A061CIP1
Application No.: 09/943,659 -Confirmation No.: 2421
Inventor: MUNDY et al.
Title: Methods of Treating Multiple Myeloma and
Myeloma-Induced Bone Resorption Using Integrin
Antagonists

EFFECT OF ACUTE TREATMENT ON TUMOR BUREN



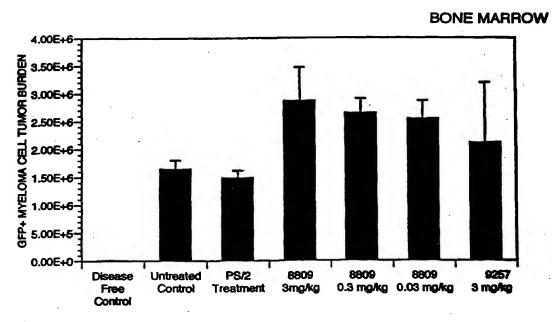
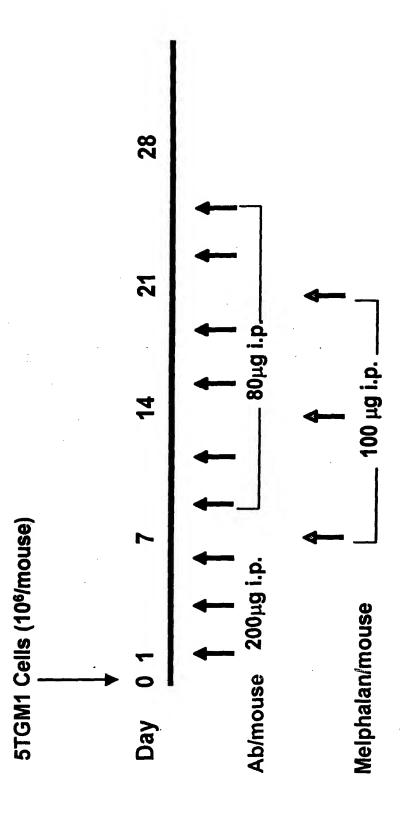


Figure 34

Experimental Protocol



Pigure 35

Docket No: A061CIP1
Application No.: 09/943,659 -Confirmation No.: 2421
Inventor: MUNDY et al.
Title: Methods of Treating Multiple Myeloma and
Myeloma-Induced Bone Resorption Using Integrin

Antagonists



Inhibition of Hindleg Paralysis

